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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,303	02/26/2004	Kelly Reed Clark	28335/40012	8089

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,303	CLARK ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/25/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14, 18, 19, 21-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,18,19 and 21-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/25/2007 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel biological materials, specifically the E3 deleted adenoviruses rAd5/E3/TRE-rep52/40-3 and rAd5/E3/TRE-rep52/40-5. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method

set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, a deposit of the biological materials may satisfy the requirements of 35 U.S.C. § 112. The specification does not disclose a repeatable process to obtain the biological material and it is not apparent if the biological materials are readily available to the public. Both recombinant adenoviruses are specific clones made by passage and selection in 293 cells. If one of skill in the art were to repeat the process of making these clones disclosed in specification, it is not predictable that the exact clones (i.e. adenoviral vectors with the exact same nucleotide sequence, and functional properties, as those recited in the claims) could be produced. The process disclosed (Example 3, or ¶'s [0038] - [0039] of the published application: US 20040224411 A1) yielded a number of adenoviral clones, not all of which expressed the desired AAV proteins, and the clones recited in the claims expressed the AAV proteins to different extents (see Fig. 2 and Example 3). Thus, practicing the disclosed method for producing the claimed adenoviruses does not necessarily yield adenoviruses with the desired properties, let alone the exact adenoviruses recited in the claims.

If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon an issuance of patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide an

affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. §§ 1.807); and

(e) the deposit will be replaced if it should ever become unviable.

Applicant's attention is directed to M.P.E.P. § 2400 in general, and specifically to §2411.05, as well as 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Natsoulis et al (U.S. Patent 6,027,931, 2000). **This rejection is maintained for reasons made of record in previous Office Actions dated 7/9/2005, 4/4/2006, 12/20/2006, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 6/25/2007 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the claims have been amended to remove the term "about" in reference to expression levels of the Rep 78/68 proteins; 2) Natsoulis et al does not teach the methods recited in claims 3 and 10, i.e. that an expression cassette encoding Rep 52/40 proteins is introduced into a cell already comprising a rAAV genome, AAV rep-cap proteins and AAV helper functions; 3) claim 18 requires infection by a naturally occurring adenovirus, a limitation not taught by Natsoulis et al.

Regarding 1), Natsoulis et al teach various constructs, shown in Fig. 1, to provide rep-cap proteins. In the case of pRCM.kozak (lane 4 in Fig.2) and pRCM.polyA (lane 5 in Fig.2), Rep78/68 expression is considered to be at the level when the proteins are under control of the AAV p5 promoter. This is because these vectors use the p5 promoter (Fig.1) and the Western

blot for Rep 78/68 shown in Fig.2 indicates equal bands for the Rep78/68 proteins (labeled A in Fig.2) with respect to the AAV control (lane 1 of Fig. 2). Furthermore, the level of Rep 52/40 expression was greater than the control (i.e. the B bands in Fig. 2) for these two vectors because the respective bands are larger and more intense than the control (again, lane 1, the AAV vector) in which the Rep52/40 proteins are under control of the p19 promoter (column 6, lines 25-31).

Regarding 2), the AAV vector and AAV helper function (i.e. the Rep/Cap constructs of Fig. 1) may be transfected into the cell sequentially (column 12, lines 39-42). The Rep 52/40 provided by the AAV helper constructs are considered "supplemental" to any encoded by the AAV vector (The AAV vector may include rep-cap coding sequences, column 6, last ¶). A review of the previous Office Actions does not reveal that the Examiner indicated Example 1 was a basis for teaching this limitation, as applicants assert (page 9 of the response).

Regarding 3), in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a naturally occurring adenovirus) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus, given a reasonably broad interpretation of the claimed subject matter, Natsoulis et al is considered to anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 26, 28, 29, 31, 35, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Hardy (U.S. Patent 6,429,001, 2002).

Claims 25 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Murphy (U.S. Patent 6,635,476, 2003, effective filing date of 10/15/1999).

Claims 27-29 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al and Hardy as applied to claims 1-3, 10-13, 18, 21-24, 26, 28-33, 35, 37, and 38 above, and further in view of Potash et al (U.S. Patent 5,911,998, 1999).

These rejections are maintained for reasons made of record in the previous Office Actions dated 7/9/2005, 4/4/2006, 12/20/2006, and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 6/25/2007 have been fully considered but they are not persuasive. Because the arguments relating to the above 35 USC §103 rejections are essentially the same, they are addressed together. Applicants essentially assert that Natsoulis et al does not teach all the instant claim limitations, and the other documents cited above do not remedy the deficiency of Natsoulis et al. This is not persuasive because for reasons set forth above, Natsoulis et al is still considered anticipatory for claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33. Therefore, it is considered the above claims are rendered obvious as set forth above and as set forth in the previous Office Actions.

Claims 4, 5, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) as applied to claims 1-3, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Collaco et al (Gene, 1999).

The teachings of Natsoulis et al are as described above and applied as before. Natsoulis et al do not teach an AAV Rep52/40 expression cassette in a recombinant adenovirus (rAd), an E3-deleted rAd, or an E1-deleted rAd.

Collaco et al teaches the production of recombinant AAV using the pSH3 and pSH5 vectors, which comprise the adenovirus E4, E2a and VA genes, and thus are considered E1 and E3 deleted recombinant adenoviruses because they do not contain the E1 and E3 adenoviral genes. The pSH3 and pSH5 vectors were used to deliver the AAV rep and cap genes. See Fig. 1

and legend, the abstract, page 398, second column, and Table 1. The instant specification does not define a recombinant adenovirus. Hence, the term is interpreted broadly to include recombinant vectors that comprise elements of the adenoviral genome, and that might function as set forth in the claims. Furthermore, claim 9, and applicants arguments (¶ linking pages 7 and 8 in the response of 6/25/2007) , indicate that a recombinant adenovirus need only retain the ability to introduce the Rep52/40 expression cassette, or viral elements necessary for a functional adenovirus vector. Collaco et al also teach that their system allows adenovirus-free production and increased yields of an AAV vector, desirable properties for AAV production. See the Discussion beginning on page 404, first column, and page 398, first column, second and third full ¶'s.

The claimed methods are essentially disclosed by Natsoulis et al with the exception of the AAV Rep52/40 expression cassette in a recombinant adenovirus (rAd), E3-deleted rAd, and E1-deleted rAd limitations. The ordinary skilled artisan, seeking a method to produce recombinant AAV in higher yields and free of adenovirus contamination, would have been motivated to use the pSH3 and pSH5 vectors with the methods and Rep/Cap expression cassettes of Natsoulis et al because Collaco et al teaches the pSH3 and pSH5 vectors to be well known and have utility for methods of introducing AAV Rep/Cap proteins and adenoviral helper functions into cells. It would have been obvious for the skilled artisan to do this because of the known benefits of increased AAV yield and adenoviral-free production of AAV, as taught by Collaco et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the

ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 9, 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al (6,027,931) and Collaco et al (Gene, 1999) as applied to claims 1-5, 8, 10-13, 18, 21, 23, 24, 30, 32 and 33 above, and further in view of Gao et al (U.S. Patent 7,235,393, effective filing date 4/29/2002) and the ATCC entry for VR-199, i.e. Simian virus 20 (of record).

The teachings of Natsoulis et al and Collaco et al are as described above and applied as before. Neither Natsoulis et al nor Collaco et al teach the use of SV-20 to complement (i.e. to provide helper functions) rAAV production.

Gao et al teaches that for the production of recombinant AAV, literally any available adenovirus would be useful, including those from simian species, such as SV-35, SV-25, etc., that are available from the ATCC. See column 4, beginning with line 4.

The ATCC entry for SV-20 indicates that it has been a well-known and available type of adenovirus since 1958 (the date of the cited reference, Hoffert et al).

The claimed methods are essentially disclosed by Natsoulis et al and Collaco et al with the exception of the SV-20 limitation. However, all of the elements recited in the claim were known in the art, and the use of SV-20 in the prior art methods is merely substituting one known element (i.e the human adenoviruses of Natsoulis and Collaco) for another (the simian adenoviruses/SV-20, as taught by Gao et al and the ATCC entry). In particular, Gao et al teaches the predictability of substituting literally any known adenovirus of human or non-human origin for use in the complementation of rAAV. Thus, the claimed invention would have been obvious

because substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633

MD Burk